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Biosurfactants can promote and stabilize protein structure. Biosurfactants fold and stabilize outer membrane proteins. The thermal stability is however perturbed in anionic biosurfactants compare to non-ionic dodecyl maltoside which is often used for membrane protein stabilization.
Upon infections, human proteins may be exposed to secreted microbial biosurfactants. Lysozyme, a defensive and antimicrobial human enzyme, is highly protease resistant. However in the presence of anionic rhamnolipid, produced by the opportunistic pathogen *Pseudomonas Aeruginosa,* the positive surface potential is neutralized and lysozyme becomes easily susceptible for both human and bacterial proteases. Rhamnolipid also promotes fibrillation of FapC, the main protein in *Pseudomonas Aeruginosa* functional amyloids. Rhamnolipid induces instant fibrillation and also morphological changes in FapC fibrils. Biosurfactants may thus play an important role in microbial biofilms and infections.
In general, biosurfactants can interact with proteins in multifarious ways with fundamental, medical and industrial relevance.

2640-Pos Board B70
Stability Analysis of CFTR via Tryptic Digestion
Christopher Holmes[1,2].
[1]University of Mount Union, Alliance, OH, USA, [2]University of North Carolina at Chapel Hill, Chapel Hill, OH, USA.
Cystic fibrosis (CF) is caused by malfunctioning cystic fibrosis transmembrane conductance regulator (CFTR). When the flow of chloride ions through the CFTR channel becomes hindered or ceases, mucus begins to accumulate within the body causing a plethora of respiratory, digestive, and reproductive complications. From the 1,500 different CFTR mutations that exist, a genetic mutation resulting from the deletion of a phenylalanine residue at the 508 position (ΔF508) has been identified as the most common. For that reason, the ΔF508 mutation has become a target for initial treatment options. Due to the transmembrane nature of CFTR and a length of 1480 residues, the crystal structure and consequently the functionality of CFTR, are still vastly unknown. The objective of this research is to more thoroughly understand the relative stability of CFTR, the ΔF508 mutant and the treated ΔF508 mutant via limited tryptic digestion and the quantification of western blots. The ΔF508 mutant was treated with an energy source in which it typically binds (ATP), a non-hydrolysable ATP analogue (AMP-PNP), and with an available cystic fibrosis treatment option (lumacaftor/VX-809). To adequately represent both of the nucleotide binding domains (NBDs) in CFTR, antibodies 660 (IGg1) and 769 (IGg2b) were used. The quantification of results indicated that the induced stability of the AMP-PNP treated and ATP treated ΔF508 CFTR were significantly greater than the ΔF508 mutant alone, but not significantly greater than the VX-809 treated CFTR.

2641-Pos Board B71
Modulation of Cytochrome C Stability during Chemical and Thermal Denaturization by Addition of Hofmeister Ions
Eric S. Peterson, Mikayla J. Freese, Sean J. Steinke.
Chemistry and Biochemistry, University of Northern Iowa, Cedar Falls, IA, USA.
The ferric cytochrome *c* (Cyt *c*) (un)folding mechanism in the presence of ions from the Hofmeister series is examined. Unfolding was initiated both thermally and with chemical denaturants. Hofmeister ions were added singly and in pairs to alter the stability of the native folded state, the unfolded state, and two partially folded intermediates. Protein stability was characterized by either the midpoint of the chemical denaturization curve or by the melting temperature in the thermal studies. UV/VIS absorption spectroscopy and a basis spectra fitting analysis were used to determine the populations of each protein conformation along the folding pathway. These species can be differentiated by their axial heme ligands. Four species exist in solution: the native HM state (His18/Met80), the partially folded HW (His18/water) and HH (His18/His33) intermediates, and the 5C (water) unfolded state. The results indicate that the thermal and chemical denaturization pathways are not the same and that both involve significant backbone rearrangement. The relative populations of the conformational states depends on how the protein is denatured. Additionally, it was found that addition of multiple ions changed the protein's stability in an additive manner. For example addition of guanidinium, which destabilizes folded structure, can be countered by addition of phosphate, which stabilizes folded structure. Both the (un)folding kinetics and the accessible conformations were found to depend on the identity of ions present. These results are discussed in terms of the hydrophobic effect, partitioning of the ions to the protein surface, and an altered water structure around the protein.

2642-Pos Board B72
Theoretical Prediction of Thermal-Stability Changes upon Mutations of a Protein
Shota Murakami[1], Hiraku Oshima[2], Tomohiko Hayashi[2], Masahiro Kinoshita[2].
[1]Kyoto University, Graduate School of Energy Science, Uji, Japan, [2]Kyoto University, Institute of Advanced Energy, Uji, Japan.
Maintaining the structure and function of a protein at a temperature above the denaturation temperature of its native state is a principal objective of researchers in a variety of fields. One of the methods of enhancing the thermal stability is the mutation. In the present study, we report the results of the first attempt to develop a theoretical approach for predicting the thermal-stability changes upon mutations of a protein without using any parameters fitted to the experimental data. The approach is based on our recently developed free-energy function wherein the water-entropy effect is treated as an essential factor. Protein folding is driven by a large gain of water entropy. The gain is ascribed to an increase in the number of accessible configurations of water which is brought primarily by an increase in the total volume available to the translational displacement of the water molecules in the bulk. This water-entropy effect can be characterized by the following: It is reasonably taken into account only by a molecular model for water; not only the water near the protein surface but also the water in the bulk makes a substantial contribution to the effect (i.e., the effect cannot be considered in terms of the water-accessible surface area alone); and the protein-water-water triplet and higher-order correlations play critical roles. Our theoretical approach can also be distinguished from the previously reported approaches in the respect that the water-entropy effect is taken into account to its full extent. Its performance is compared with that of FOLD-X, one of the most popular approaches using the fitting parameters, for ten proteins and single and multiple mutations. Ours is shown to be superior to FOLD-X.

2643-Pos Board B73
Tuning of Alpha-Synuclein Aggregation by Small Molecules and Bacterial Proteins
Pernilla Wittung-stafshede.
chemistry, Umeå Univeristy, umeå, Sweden.
Parkinson's disease affects a growing number of the population and involves motor complications due to the death of dopamine neurons. Cytosolic inclusions containing amyloid fibrils of α-synuclein are a hallmark of the disease and it is believed that the aggregation process (going from monomers to amyloid fibers) of alpha-synculein somehow causes neurodegeneration. The synuclein-rich inclusions share structural characteristics with amyloid fibers found in many other neurodegenerative disorders. In addition, many organisms employ amyloid structures for mechanical or biological functions; for example, amyloid fibers are the major component of microbial biofilms. Mature amyloid fibers of alpha-synculein may not be the source of cytotoxicity; instead, transient oligomeric structures may be most dangerous to the neuronal cells. To investigate molecular pathways leading to alpha-synculein amyloid fibers, and thereby get hints for how to combat Parkinson's disease in vivo, we have taken a unique approach that involves purified proteins, biophysical experiments in vitro, and small-molecule tools. We have found that strategic ring-fused 2-pyridone compounds (mimics of small peptides), can tune alpha-synuclein aggregation such that either inhibitory or templating oligomers accumulate. Moreover, a fine balance between templation and inhibition processes is evident since one particular 2-pyridone inhibits bacterial amyloid formation but promotes alpha-synuclein amyloid fibers. In analogy with the small molecule tools, we found that bacterial proteins can cross-react with alpha-synculein and inhibit as well as promote amyloid fiber formation at sub-stoichiometric levels. Direct interactions of alpha-synculein with bacterial proteins and/or natural metabolites may play a role in controlling Parkinson's disease in humans.

2644-Pos Board B74
Ezrin is a Potent Modulator of Alpha-Synuclein Oligomerization
Timea E. Illes-Toth[1], Maliha Shah[2], Nelson Wu[1], Silvia Verzini[3], Philipp Selenko[3], Erich Wanker[2].
[1]Biomedical Engineering, Washington University in St Louis, St Louis, MO, USA, [2]Dept of Neuroproteomics, Max-Delbrueck Centrum, Berlin, Germany, [3]Leibniz Institute of Molecular Pharmacology (FMP), Berlin, Germany.
Alpha-synuclein oligomers are associated with toxicity in Parkinson's disease. Different forms of alpha-synuclein (aS) have been described, some of which can destabilize lipid bilayers, and seed the formation of fibrillar assemblies. Therapeutic interventions such as molecular chaperones and small molecule